

Applicant : Nariyoshi Shinomiya et al.
For : *c-met* siRNA ADENOVIRUS VECTORS INHIBIT CANCER CELL
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In the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (currently amended) An interfering RNA (RNAi) molecule having a sequence that is sufficiently complementary to a sequence of mRNA encoded by human *c-met* (SEQ ID NO:1), murine *c-met* (SEQ ID NO:[2]]3), or *c-met* of another mammalian source, so that expression of said RNAi molecule in a cell that normally expresses *c-met* results in diminution or loss of expression of said mRNA.
2. (original) The RNAi molecule of claim 1 that is a single stranded siRNA that forms a hairpin structure.
3. (original) The RNAi molecule of claim 1 that is a double stranded siRNA.
4. (previously presented) The RNAi molecule of claim 1 that (i) comprises, or (ii) hybridizes to a Met target sequence that comprises, a sequence selected from the group consisting of: (a) SEQ ID NO:9; (b) SEQ ID NO:10; (c) SEQ ID NO:11; (d) SEQ ID NO:12; (e) SEQ ID NO:13; (f) SEQ ID NO:14; (g) SEQ ID NO:15; (h) SEQ ID NO:16; (i) SEQ ID NO:17; and (j) SEQ ID NO:18.
5. (previously presented) The RNAi molecule of claim 1 that consists essentially of:
(i) a sequence, selected from the group consisting of (a) SEQ ID NO:9; (b) SEQ ID NO:10; (c) SEQ ID NO:11; (d) SEQ ID NO:12; (e) SEQ ID NO:13; (f) SEQ ID NO:14; (g) SEQ ID NO:15; (h) SEQ ID NO:16; (i) SEQ ID NO:17; and (j) SEQ ID NO:18, or (ii) a sequence that hybridizes to a Met target selected from (a)- (j), above.

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6. (original) The RNAi molecule of claim 4 that comprises a sequence complementary to human *c-met* mRNA which is selected from the group consisting of SEQ ID NO:13, SEQ ID NO:14, and SEQ ID NO:15.

7. (original) The RNAi molecule of claim 5 that consists essentially of a sequence complementary to human *c-met* mRNA which is selected from the group consisting of SEQ ID NO:13, SEQ ID NO:14, and SEQ ID NO:15.

8. (previously presented) A DNA molecule encoding the RNAi molecule of claim 1.

9. (previously presented) An expression construct comprising DNA that encodes the RNAi molecule of claim 1 operatively linked to a promoter that drives the expression of said RNAi in a *c-met*-expressing cell.

10. (original) An expression construct comprising the DNA molecule of claim 8.

11. (previously presented) The expression construct of claim 9, wherein a promoter is one that drives the expression of said RNAi in a *c-met*-expressing tumor or cancer cell.

12. (previously presented) The expression construct of claim 11 wherein the promoter is a polIII promoter.

13. (original) The expression construct of claim 12 wherein the polIII promoter is a U6 promoter.

14. (previously presented) A viral vector comprising the expression construct of claim 9.

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15. (previously presented, withdrawn) The viral vector of claim 14 that is a transient expression vector.
16. (original) The viral vector of claim 13 that is a stable expression vector.
17. (previously presented) The viral vector of claim 14 that is an adenoviral vector.
18. (original) The adenoviral vector of claim 17 that is an Ad5 viral vector.
19. (original) The Ad5 viral vector of claim 18 selected from the group consisting of: (a) si-mMet-Ad5⁵⁷; (b) si-mMet-Ad5⁶⁰; (c) si-mMet-Ad5¹¹⁰; (d) si-mMet-Ad5¹⁷⁸; (e) si-hMet-Ad5¹⁶; (f) si-hMet-Ad5⁶²; (g) si-hMet-Ad5²²¹; (h) si-dMet-Ad5¹¹¹; (i) si-dMet-Ad5¹⁹⁷; and (j) si-dMet-Ad5²²³.
20. (original) The Ad5 viral vector of claim 19 wherein the vector is si-hMet-Ad5¹⁶; si-hMet-Ad5⁶²; or si-hMet-Ad5²²¹.
- 21-37. (canceled)
38. (previously presented) A method of treating a *c-met*⁺ tumor or cancer in a subject, comprising administering to the subject by an effective route, an amount of the viral vector of claim 14 effective for inhibiting expression of *c-met* and thereby (i) inhibiting the growth, invasion or metastasis of cells of said tumor or cancer, or (ii) killing said tumor or cancer cells.
- 39-47. (canceled)
48. (new) The method of claim 38 wherein the tumor or cancer is glioblastoma, prostate or gastric.

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49. (new) A method of treating a *c-met*⁺ tumor or cancer in a subject, comprising administering to the subject by an effective route, an amount of the viral vector of claim 19 effective for inhibiting expression of *c-met* and thereby (i) inhibiting the growth, invasion or metastasis of cells of said tumor or cancer, or (ii) killing said tumor or cancer cells.

50. (new) The method of claim 49 wherein the tumor or cancer is glioblastoma, prostate or gastric.